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Fig.1

## A: Standard SERS      B: The COIN Concept

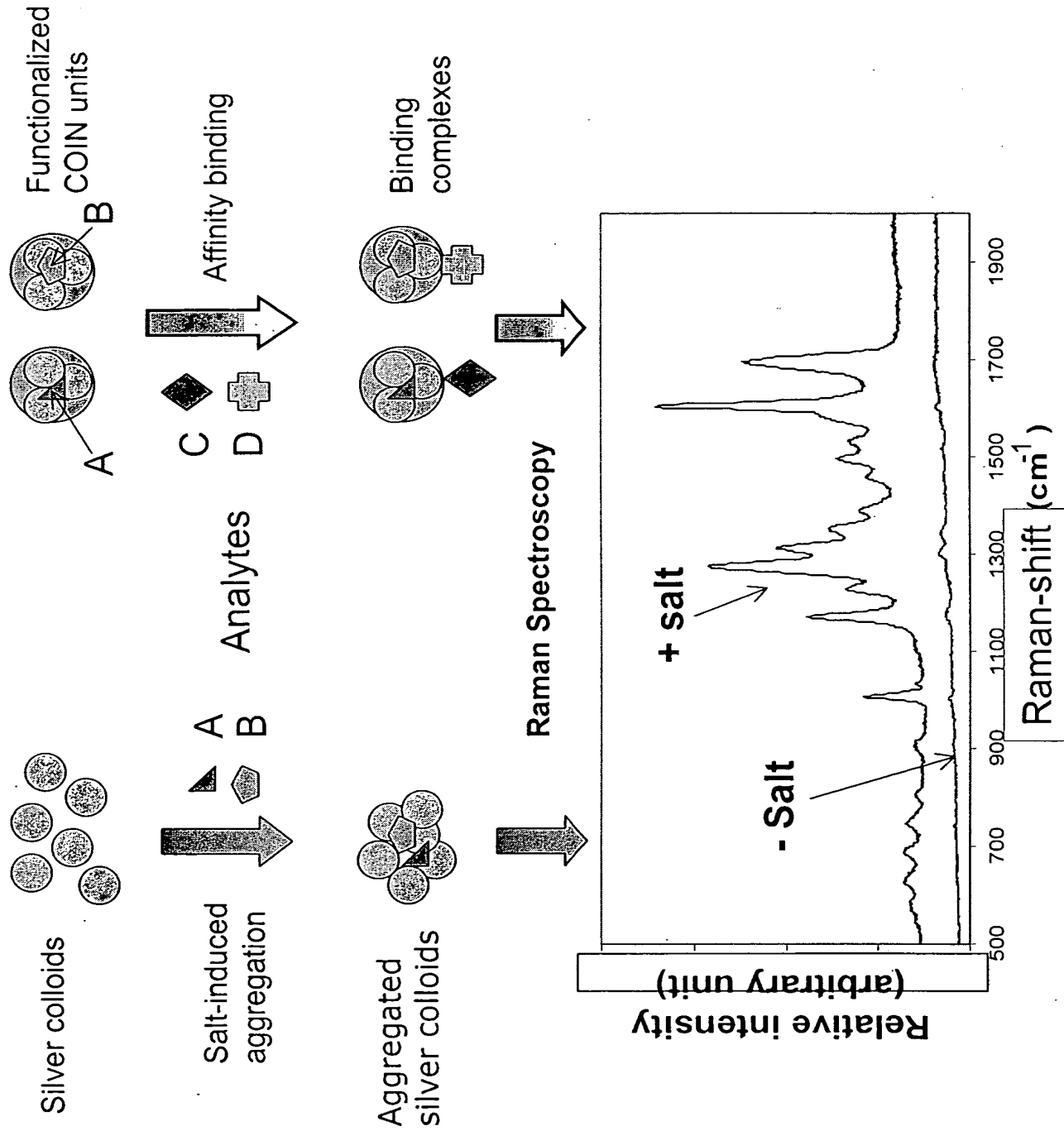


Fig. 2

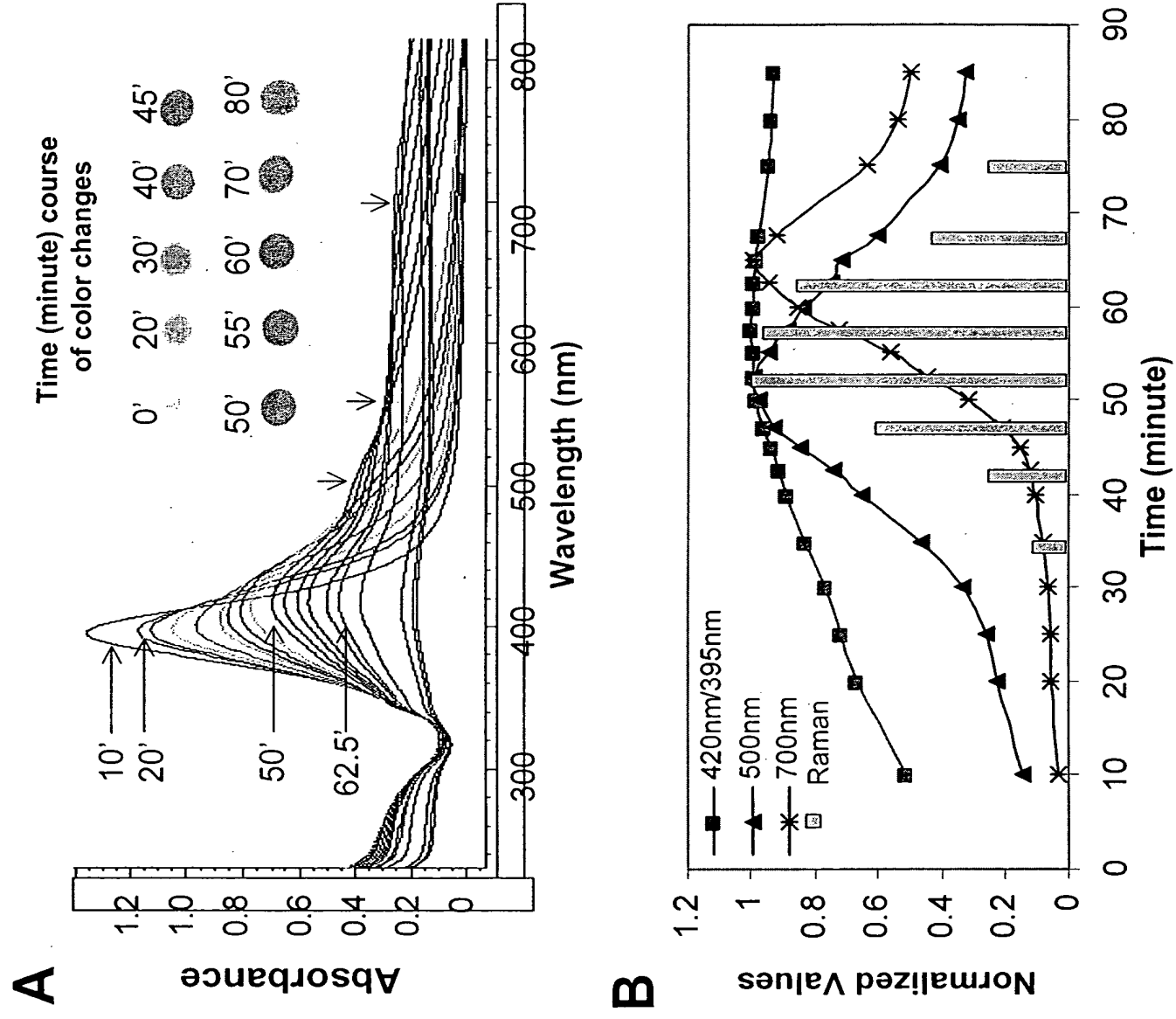


Fig. 3

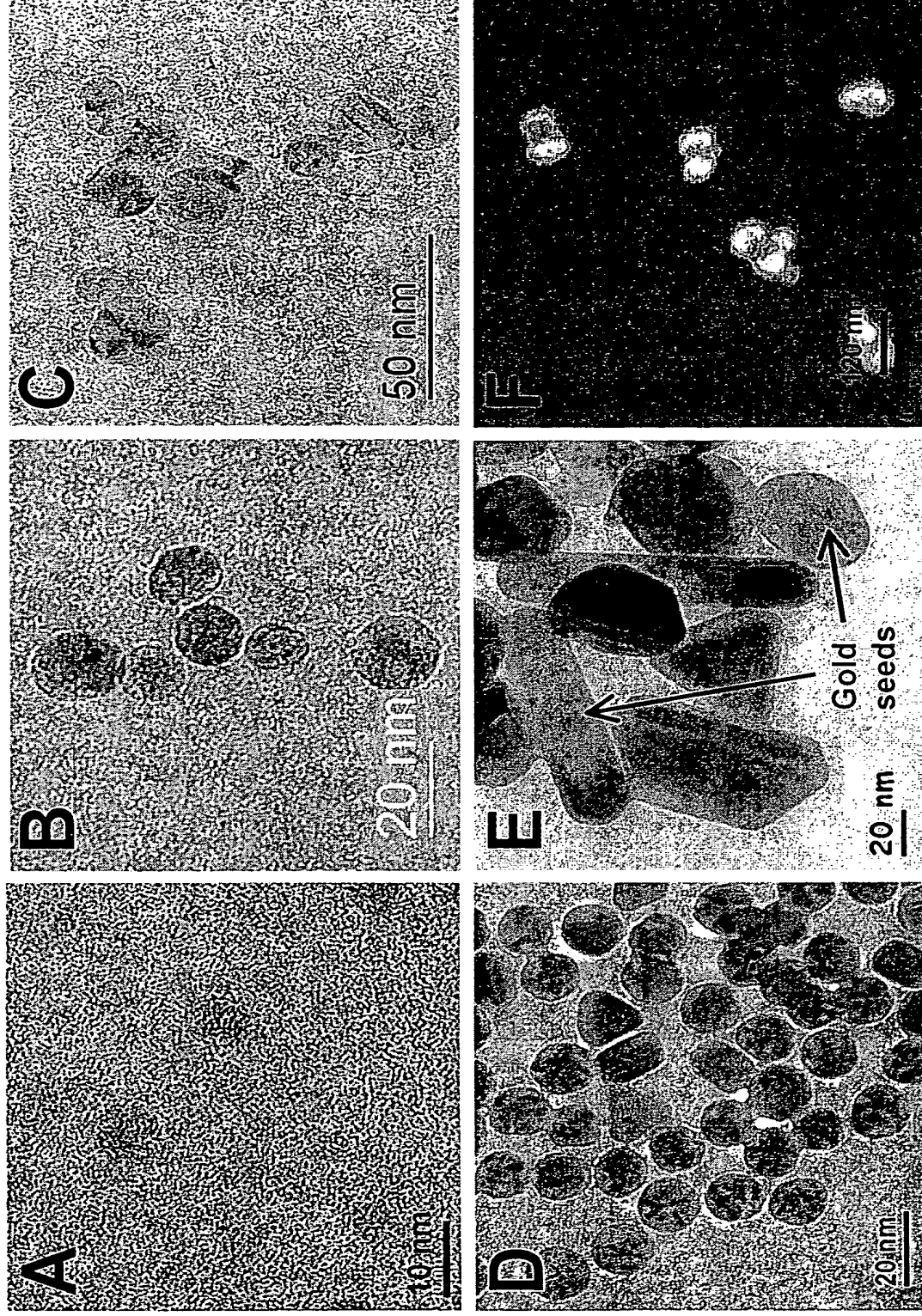


Fig. 4

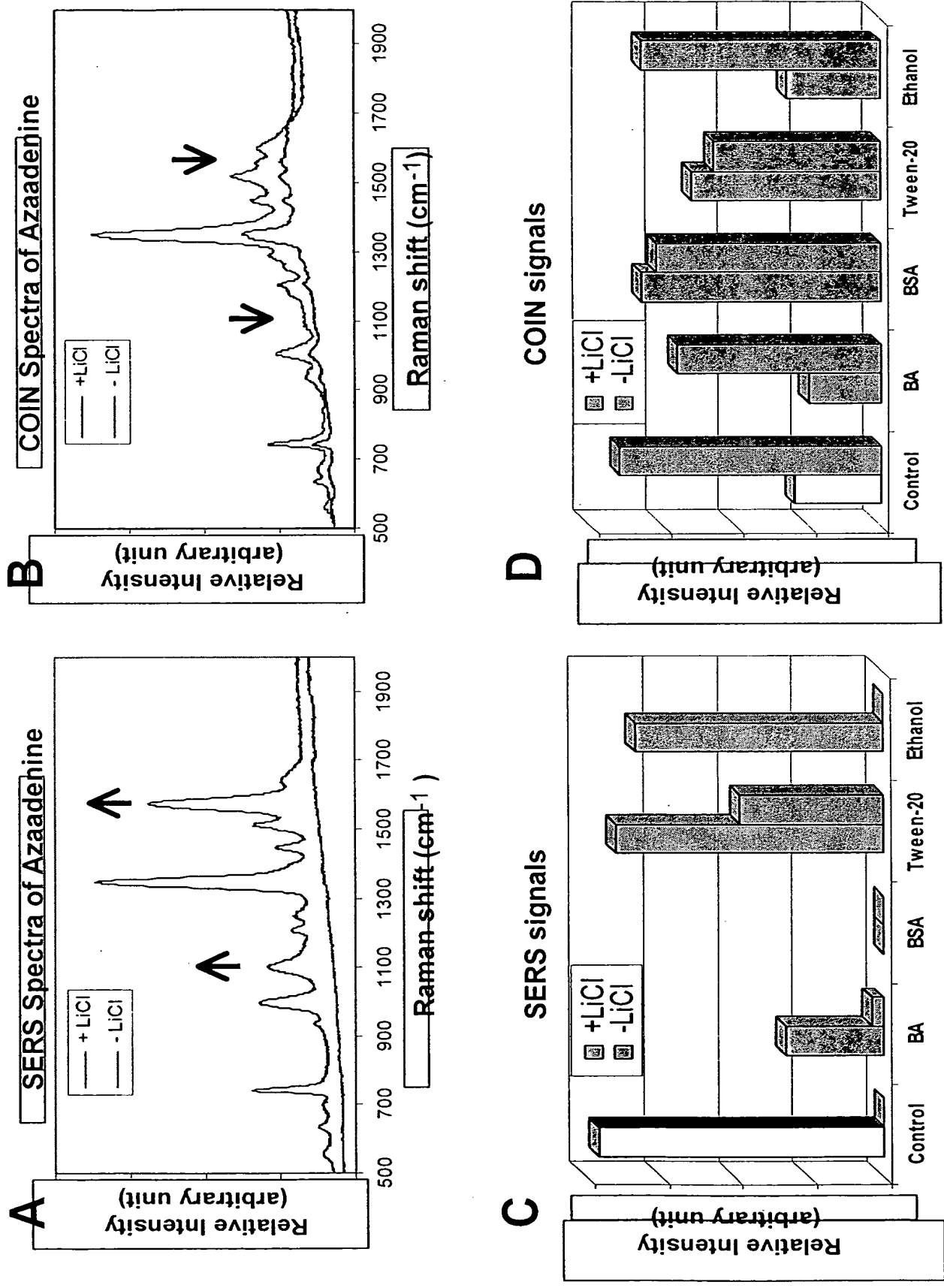


Fig. 5

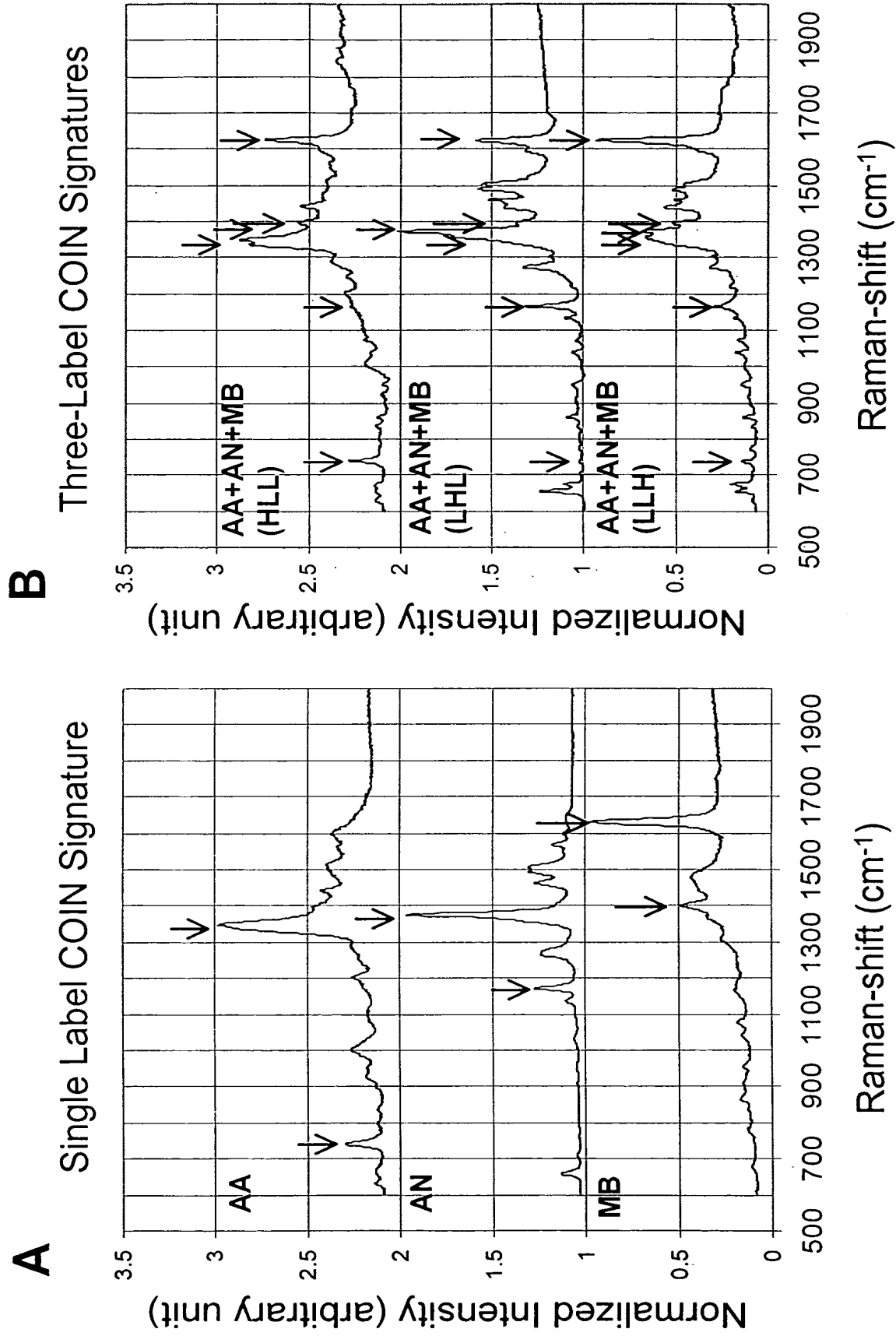


Fig. 6

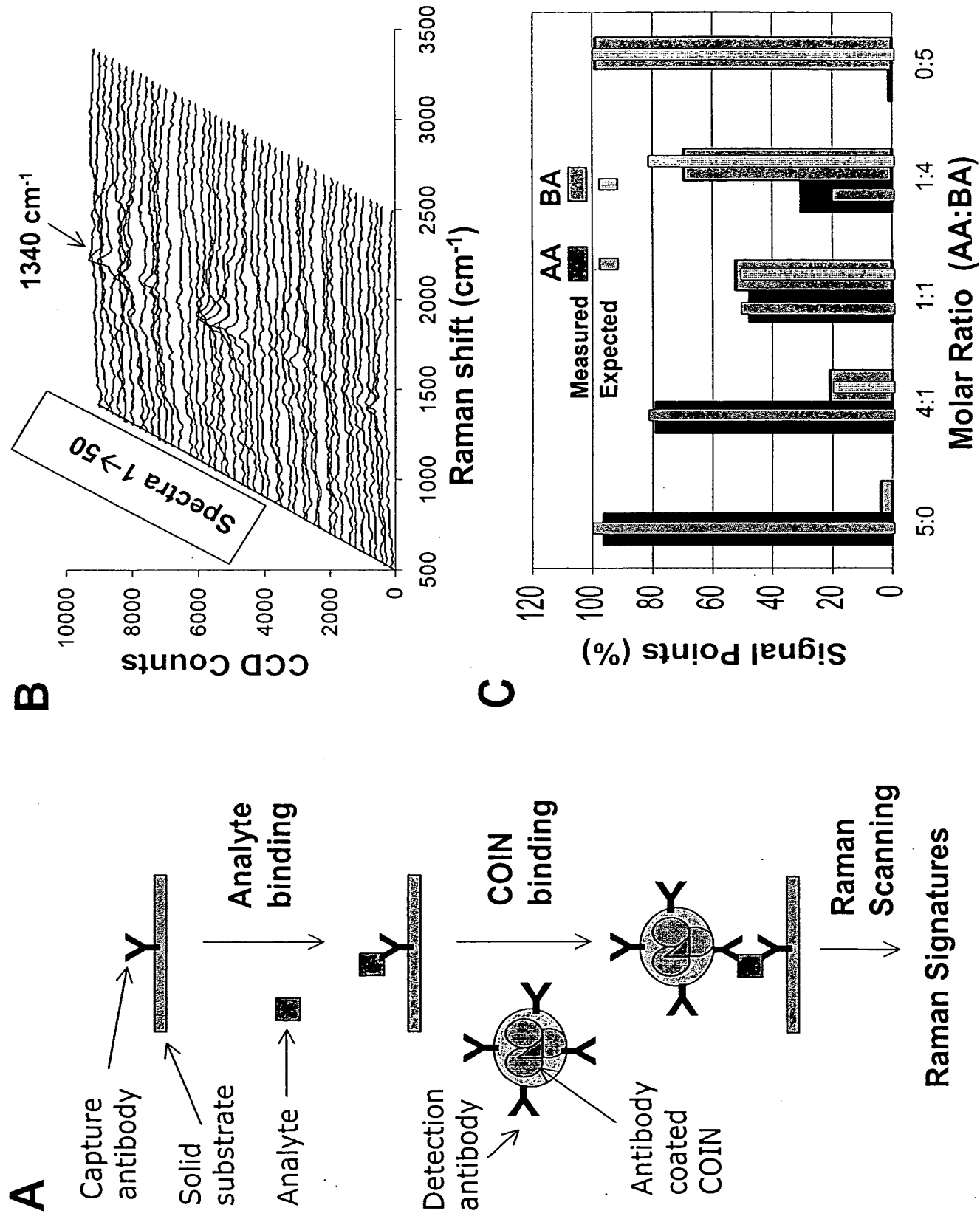
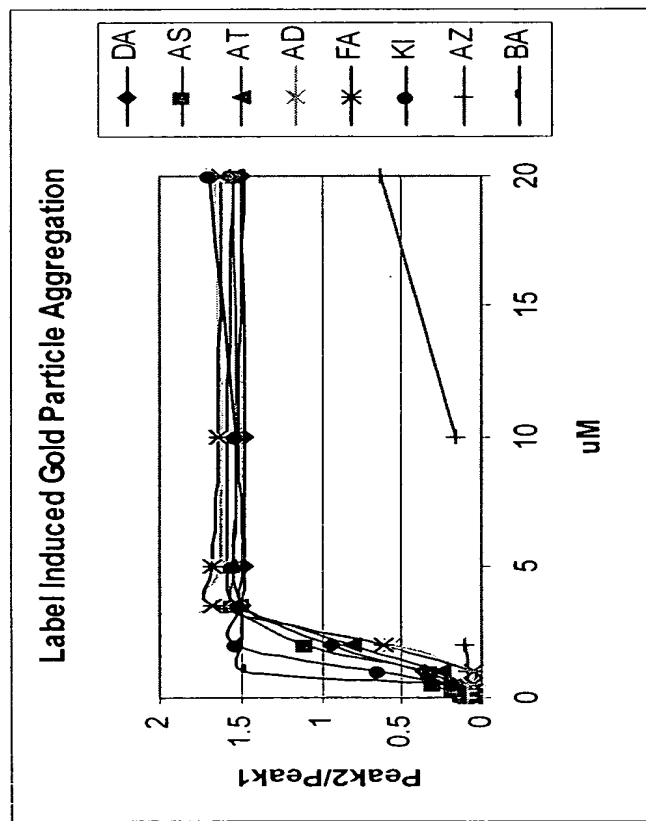


FIG. 7

**A**



**B**

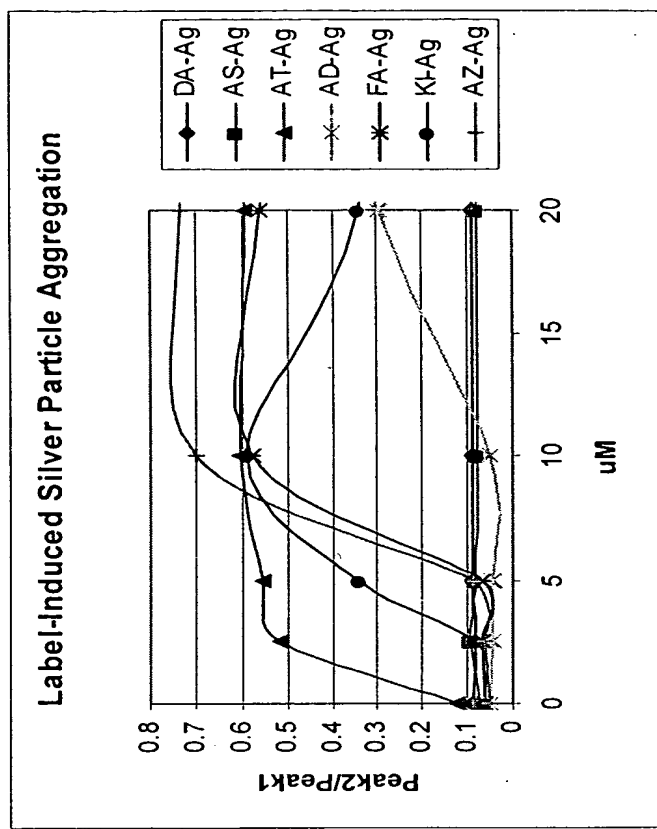




FIG. 8

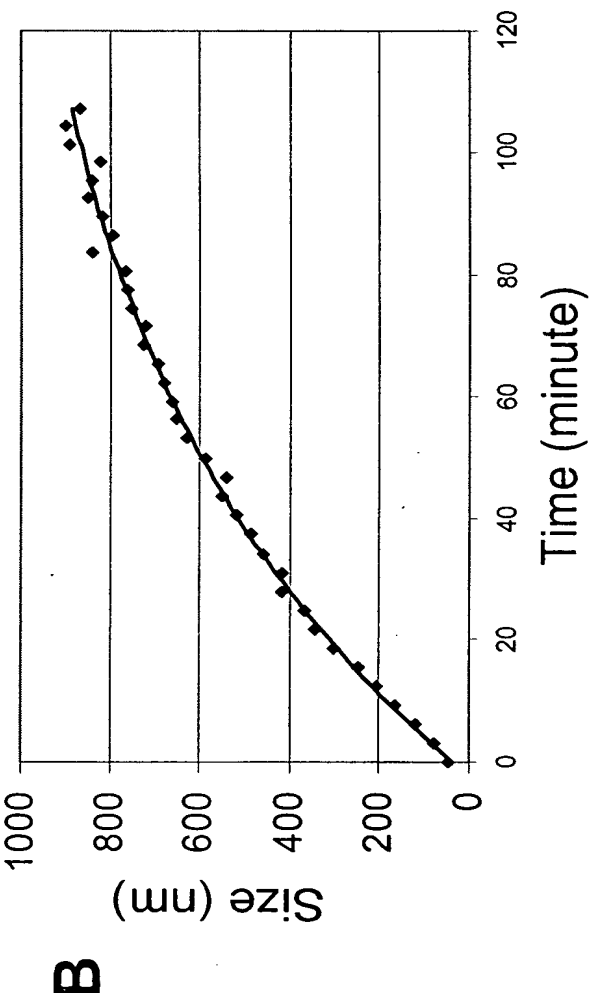
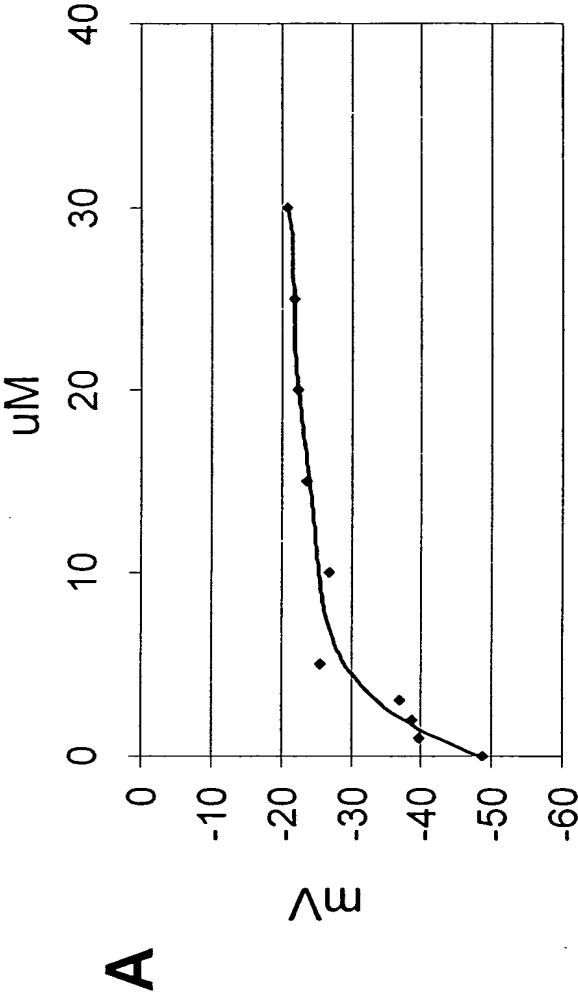


FIG. 9

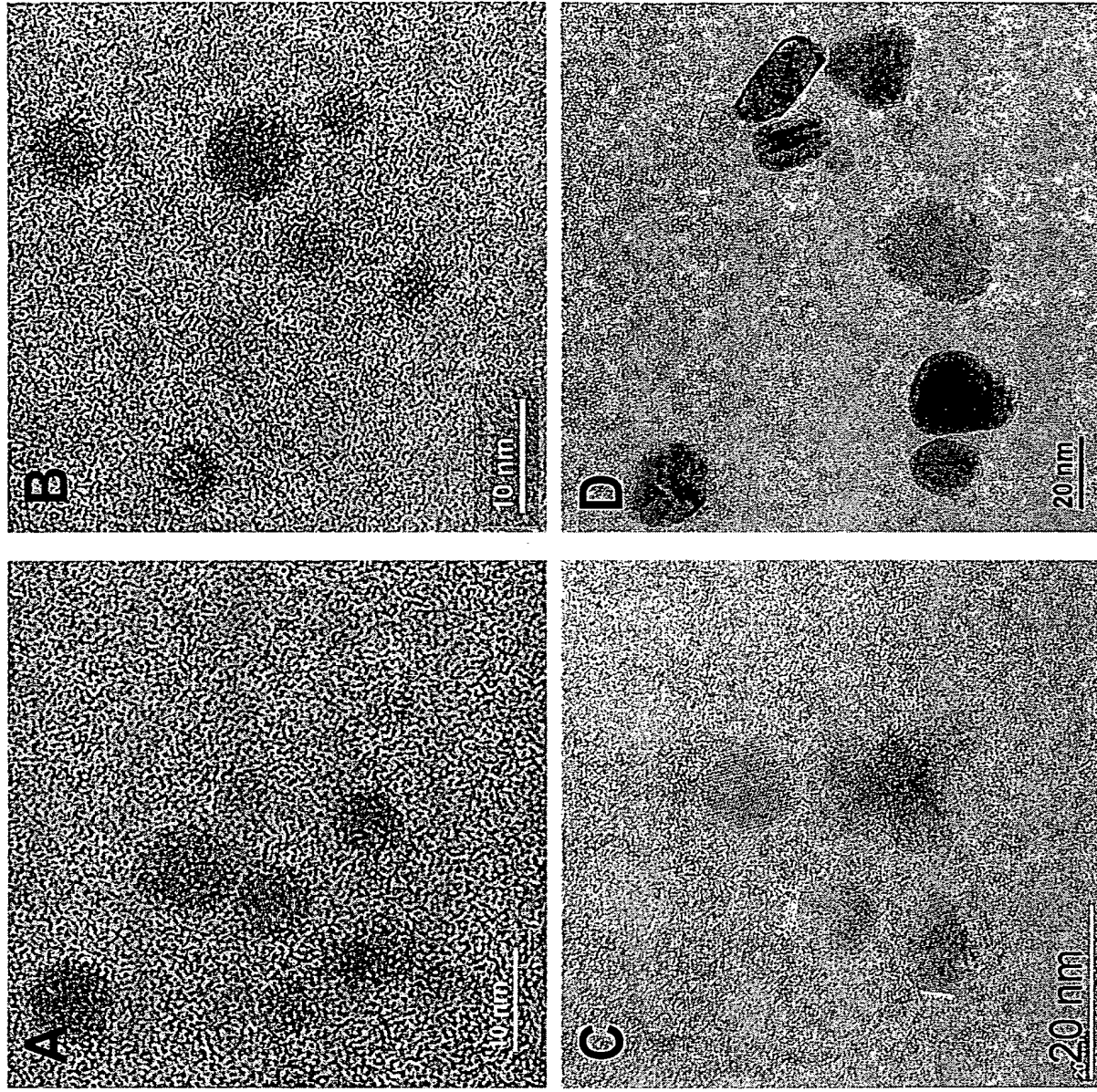


FIG. 10A

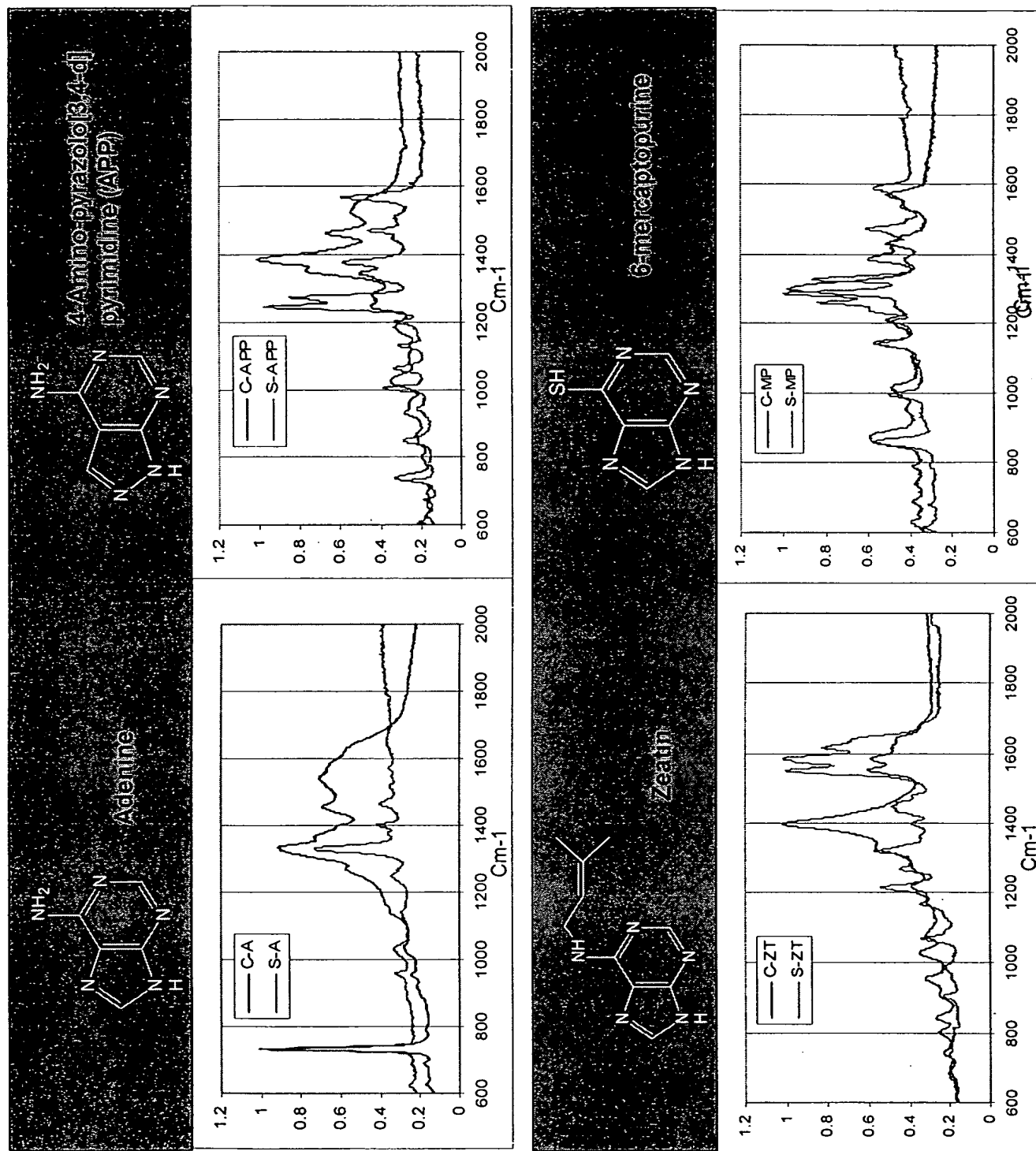


FIG. 10B

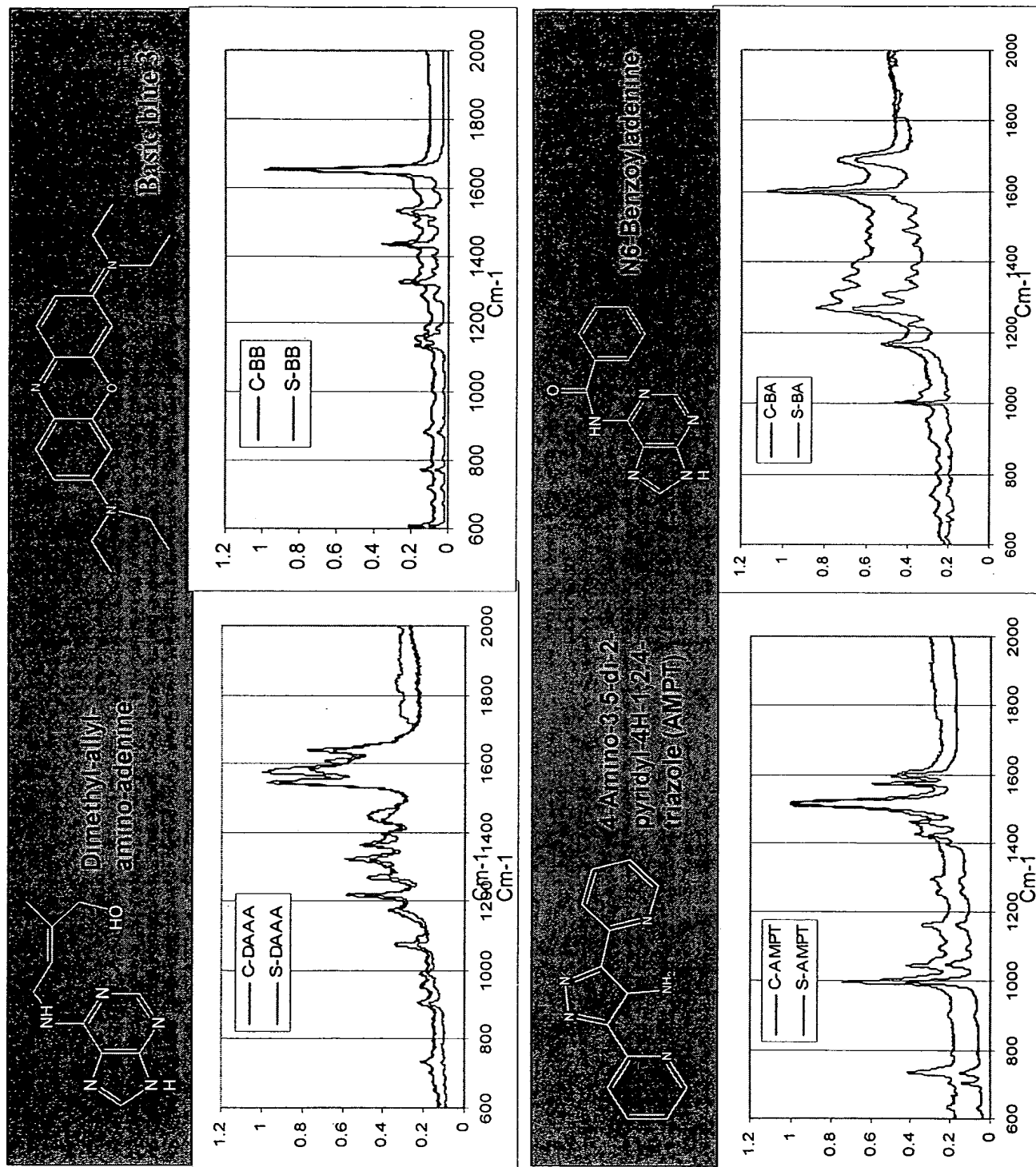


FIG. 11A

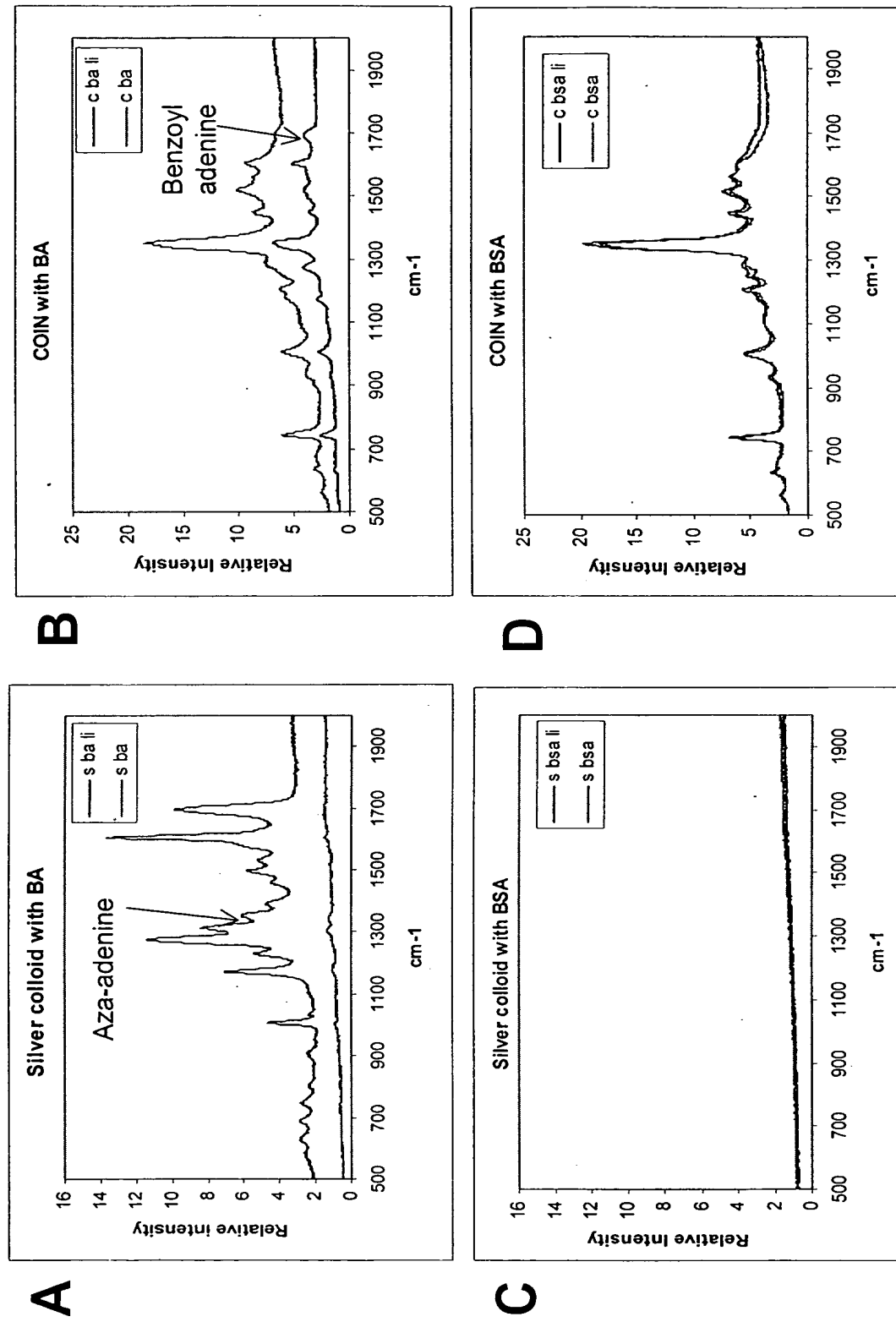


FIG. 11B

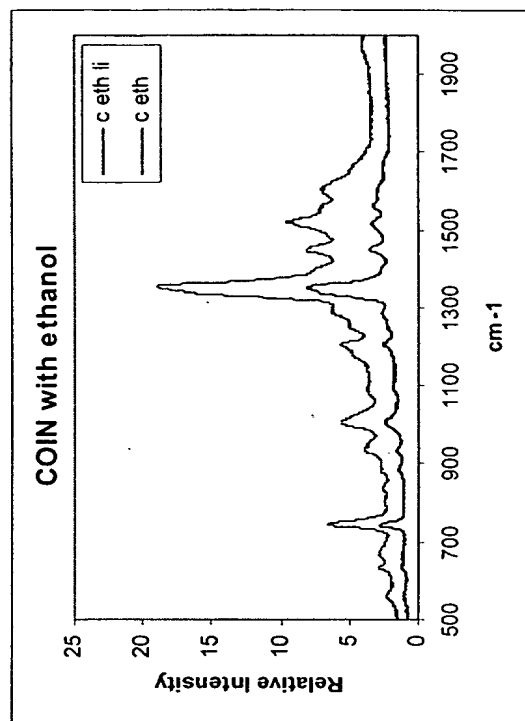
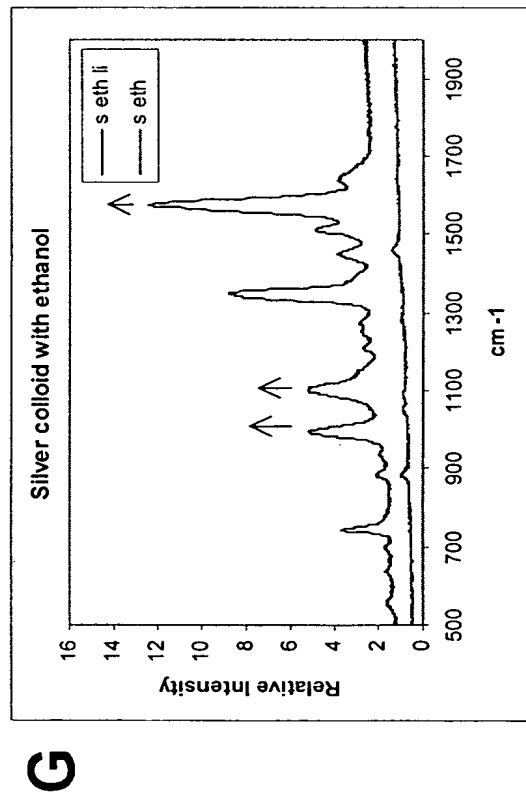
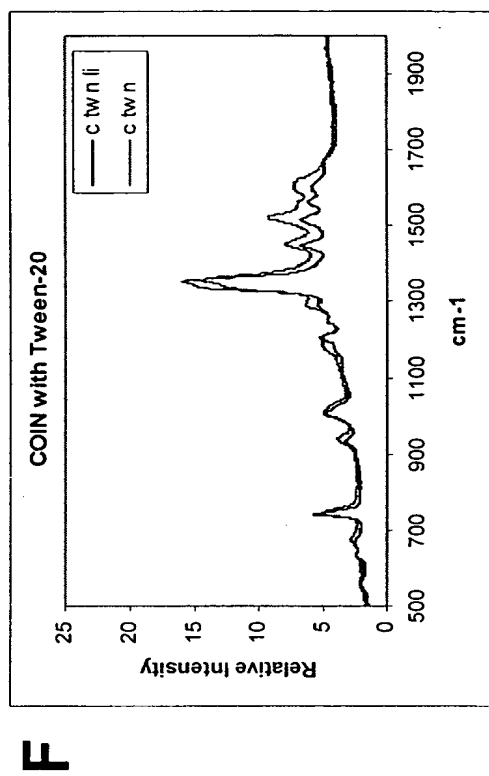
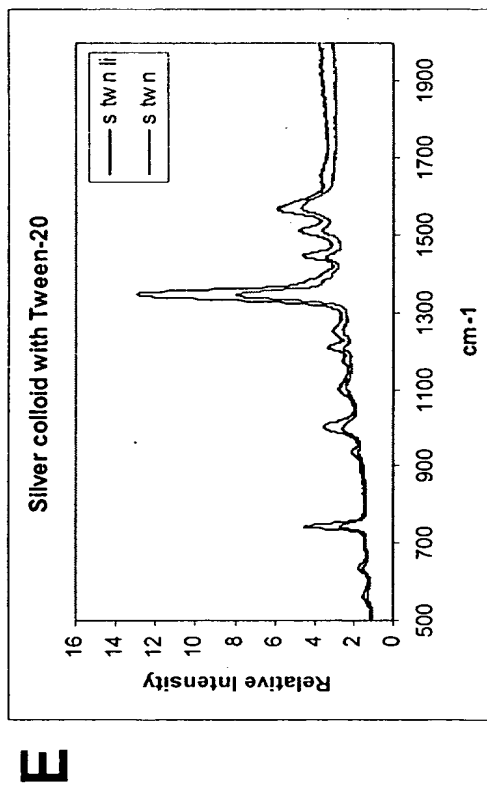


FIG. 12

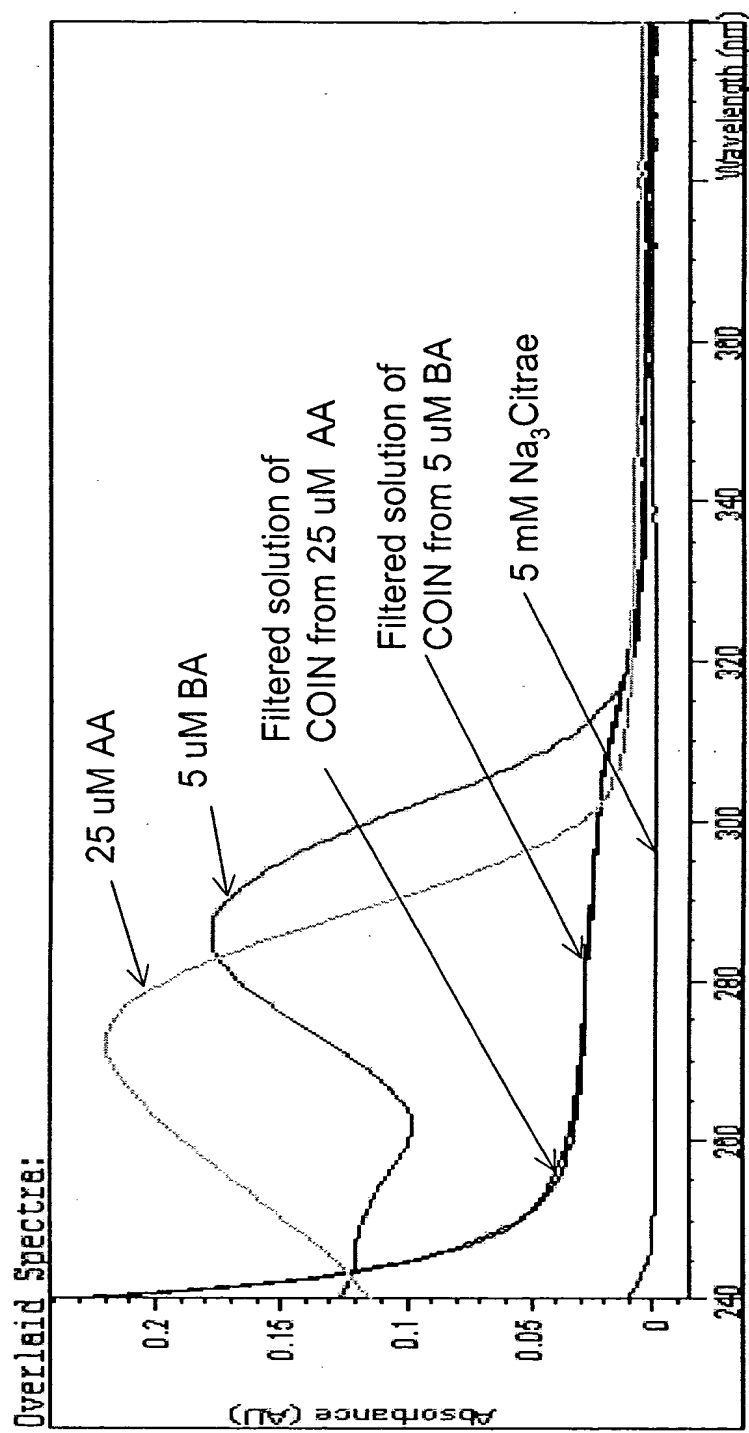
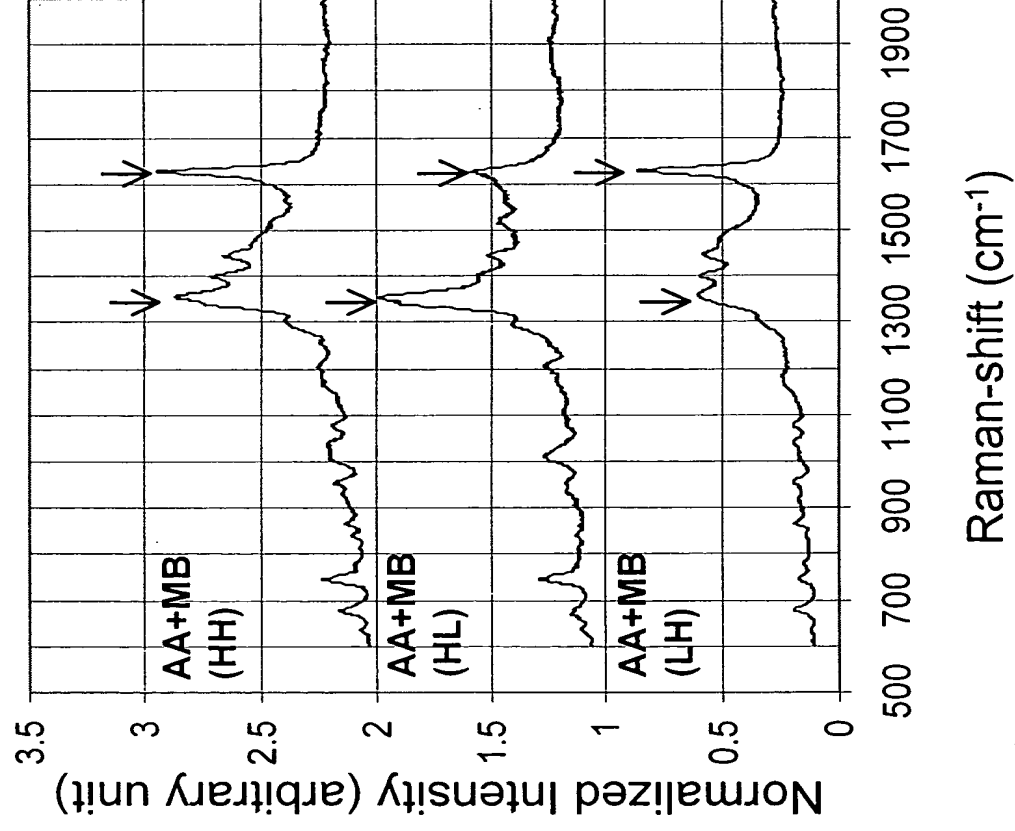


FIG. 13

**A**

Two-Label COIN Signatures



**B**

Three-Label COIN signatures

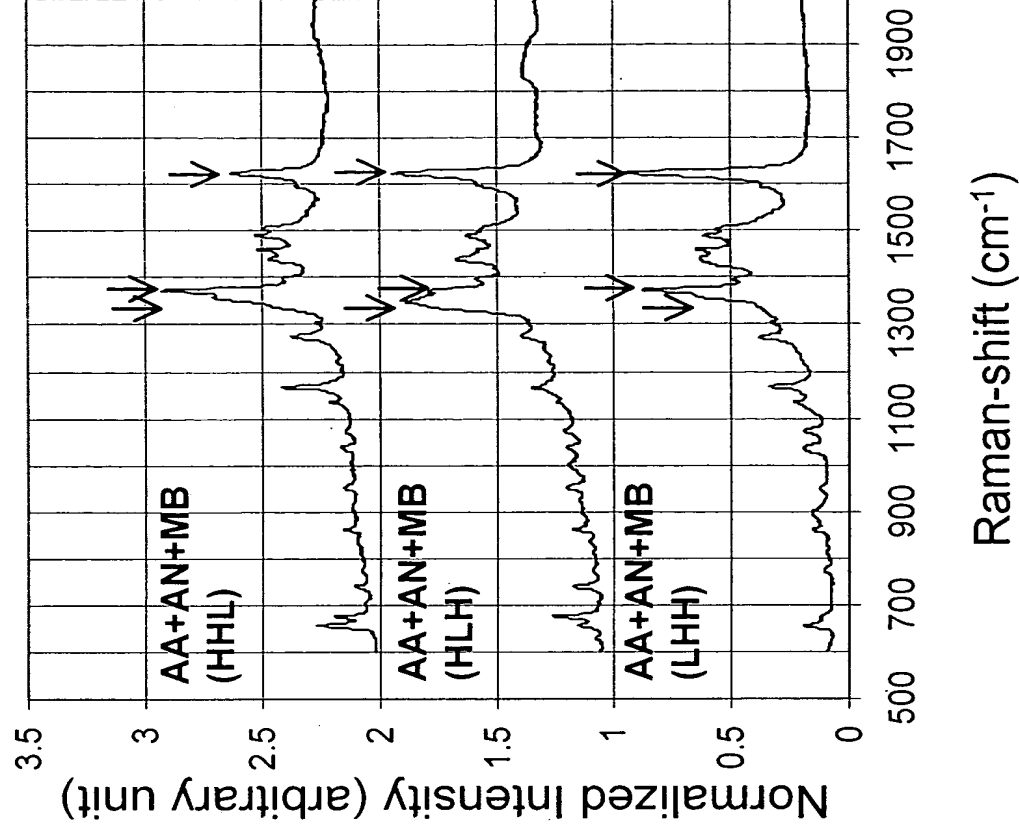
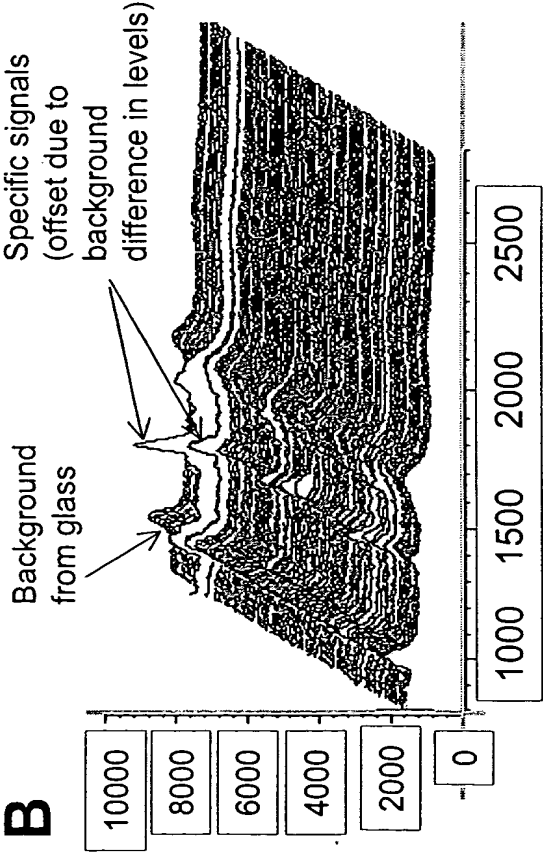
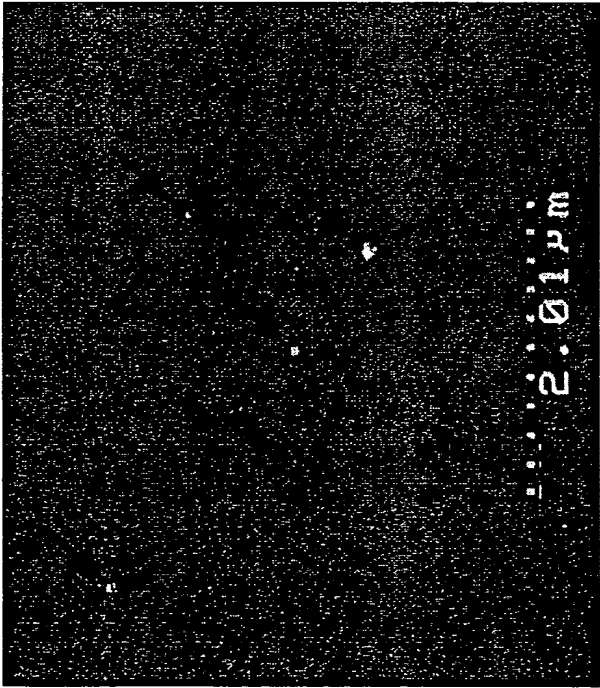




FIG. 14



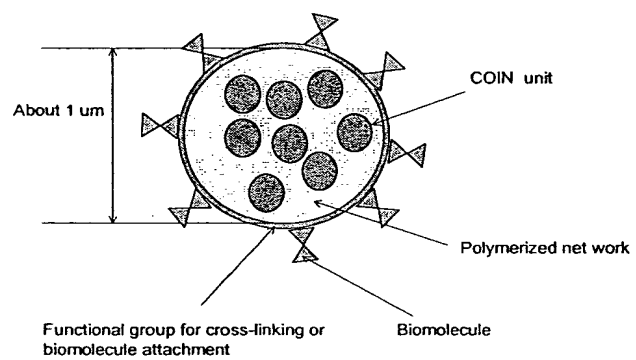
**C**

	Scanning electronic microscopic (SEM) image	Raman Scanning
Total images or spectra	40 images, 50 uM <sup>2</sup> /image	500 spectra, each covering 12 uM <sup>2</sup>
Total analyzed area (uM <sup>2</sup> )	2000	6000
Positive spectra or signal points (>50 uM for SEM)	280	259
Signal point per uM <sup>2</sup>	0.14	0.043
% Raman-active /SEM particles		30%

Table S1: Tested Organic Compounds

Organic Compound	Abbreviation	Molecular weight	Main Raman Shift Peak from COIN
Coloreless			
2-Aminopurine	AP	135.1	797 $\text{cm}^{-1}$
2-Fluoroadenine	FA	153.1	1387 $\text{cm}^{-1}$
4-Amino-pyrazolo[3,4-d]pyrimidine	APP	135.1	1345 $\text{cm}^{-1}$
4-Pyridinecarboxaldoxime	PCA	122.1	Not detected
8-Azaadenine	AA	136.1	1340 $\text{cm}^{-1}$
Adenine	A	135.1	730 $\text{cm}^{-1}$
4-Amino-3,5-di-2-pyridyl-4H-1,2,4-triazole	AMPT	238.2	1513 $\text{cm}^{-1}$
6-( $\gamma$ -Dimethylallylamino)purine	DAAP	203.2	1575 $\text{cm}^{-1}$ , 1549 $\text{cm}^{-1}$
Kinetin	KN	215.2	1531 $\text{cm}^{-1}$
N6-Benzoyladenine	BA	239.2	1600 $\text{cm}^{-1}$
Zeatin	ZT	219.2	1317 $\text{cm}^{-1}$
Colored			
4-Amino-2,1,3-benzothiadiazole	ABT	151.2	Not detected
Acridine	AF	259.7	1565 $\text{cm}^{-1}$
Basic blue 3	BB	360.9	1649 $\text{cm}^{-1}$
Methylene Blue	MB	319.9	1630 $\text{cm}^{-1}$
Thiol			
2-Mercapto-benzimidazole	MBI	150.2	1270 $\text{cm}^{-1}$
4-Amino-6-mercaptopyrazolo[3,4-d]pyrimidine	AMPP	167.2	1370 $\text{cm}^{-1}$
6-Mercaptopurine	MP	152.2	1296 $\text{cm}^{-1}$
8-Mercaptoadenine (adenine thiol)	AT	167	1331 $\text{cm}^{-1}$
Fluorescent			
9-Aminoacridine	AN	248.7	1375 $\text{cm}^{-1}$
Cyanine dyes	Cy3	466	High background (514nm laser)
Ethidium bromide	Ebr	394.3	High background (514nm laser)
Fluorescein	FAM	332.3	High background (514nm laser)
Rhodamine Green	R110	380.8	High background (514nm laser)
Rhodamine-6G	R6G	479	High background (514nm laser)

FIG. 16



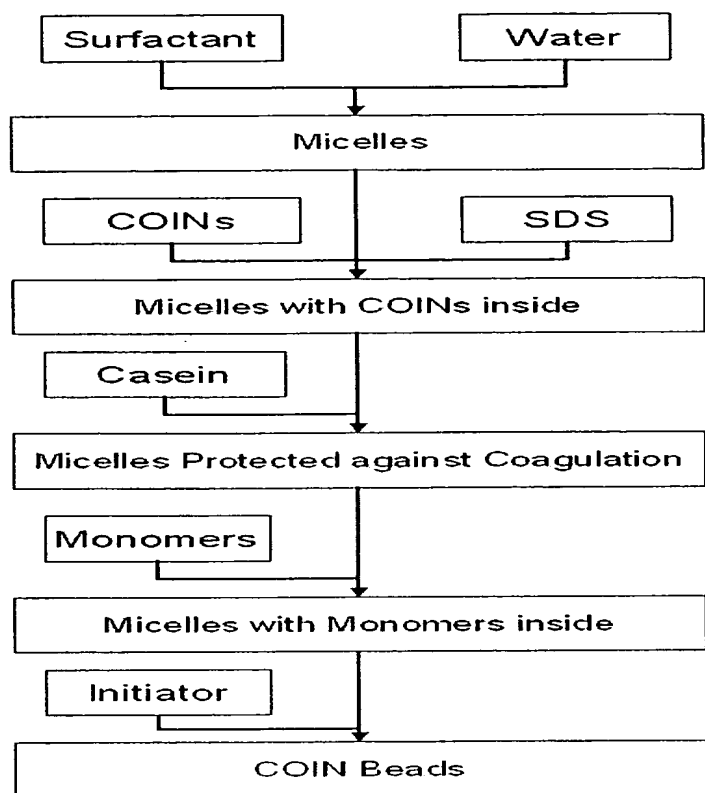


Figure 17

## Soak-in method

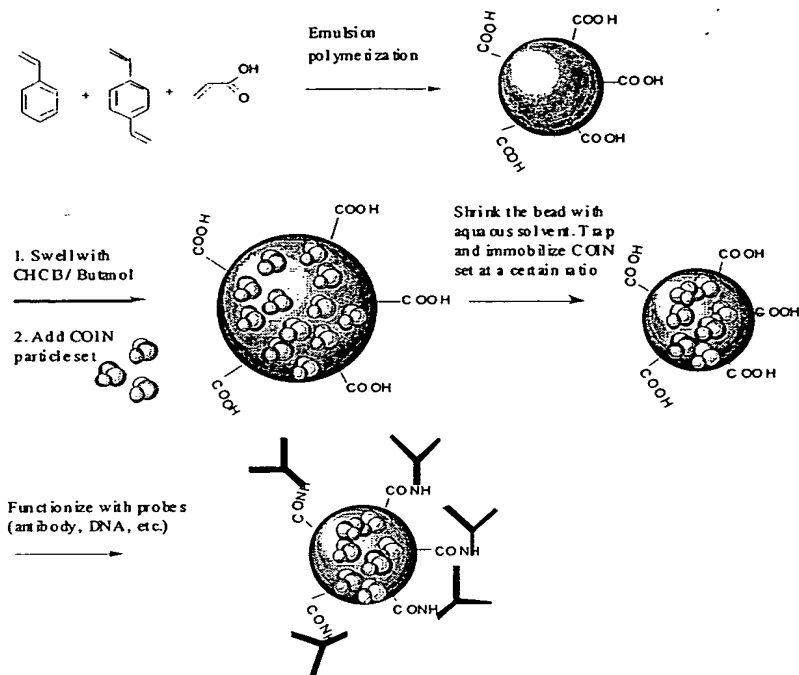
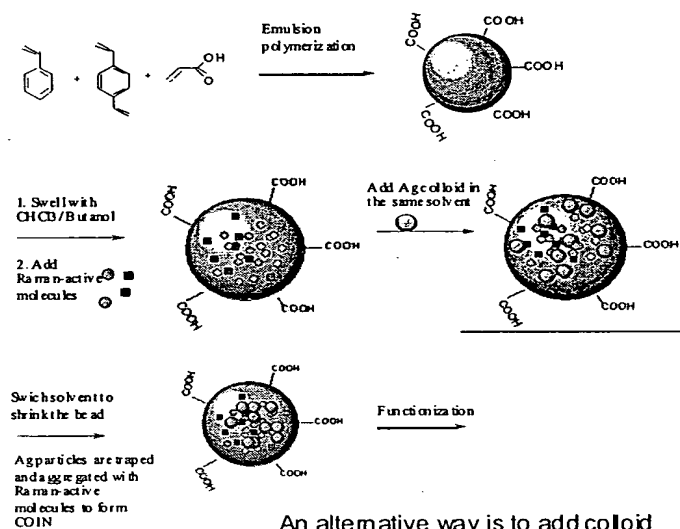


Figure 18

## Build-in Method



An alternative way is to add colloid first and then add Raman labels

Figure 19

### Build-out Method

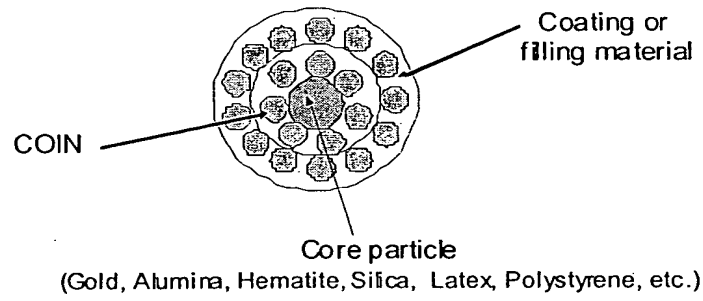


Figure 20